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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,095	03/18/2004	Nasrin Mesaeli	81190-2602	1202

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,095	MESAELI, NASRIN	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-19* is/are pending in the application.

4a) Of the above claim(s) *6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the First Office Action on the Merits on August 29, 2005. Claims 1, 3, 4, are amended. Claims 2 and 5 are cancelled. Claims 6-11 are withdrawn. Claims 12-19 are new.

Claims 1, 3, 4, 12-19 are under consideration.

Specification

Regarding the Applicant's Specification Amendments in paragraph 1, page 1 of Applicant's Remarks, filed August 29, 2005, the Examiner acknowledges that the Applicant has corrected the specification to indicate that the sense and antisense nucleotide sequences correspond to 1917-1937 of SEQ ID NO. 1.

Regarding the Applicant's Specification Amendments in paragraphs 2-4, page 1 of Applicant's Remarks, filed August 29, 2005, the Examiner acknowledges that the corrections to the Specification were to correct typographical errors.

Withdrawn Rejections

35 U.S.C. § 102(b)

Applicant's arguments, see page 5 of Applicant's Remarks, filed August 29, 2005, with respect to the rejection of claims 1 and 4 under 35 U.S.C. § 102(b) have been fully considered and are persuasive. Applicant has amended the claims. The rejection of claims 1 and 4 has been withdrawn.

35 U.S.C § 103(a)

Applicant's arguments, see pages 5 and 6 of Applicant's Remarks, filed August 29, 2005, with respect to the rejection of claims 1, 3, 5 under 35 U.S.C § 103(a) have been fully considered and are persuasive. Applicant points out that restenosis, taught by Li, et al. is not the same as hemangioma. Further, the Applicant points out that Li et al. teach injection of CRT protein and not a transgene. The rejection of claims 1, 3, 5 has been withdrawn.

New and Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 15, 16, 17 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 4 is drawn to a method of producing a transgenic mouse "having symptoms similar to hemangioendothelioma." According to the specification, "hemangioendothelioma" refers to proliferative and neoplastic vascular lesions,

including hemangiomas (specification, page 10, 4th parag.). The specification teaches that the transgenic SMCRT mice exhibit hemangioma which can be detected on the skin (specification, page 15). However, nothing in the specification teaches that the claimed mice exhibit symptoms "similar to hemangioendothelioma," nor does the specification provide guidance as to what characteristic comprise symptoms that are similar to hemangioendothelioma, but not hemangioendothelioma, itself. That is, nothing in the specification provide guidance between the difference between hemangioendothelioma and "similar to hemangioendothelioma" such that an artisan could recognize what is meant by "similar to hemangioendothelioma." Claims 15, 16, 17 depend on claim 4.

Claims 1, 3, 4, 12-17 remain rejected in part under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) a transgene comprising a nucleic acid sequence encoding mouse calreticulin (SEQ ID NO. 23) operably linked to a mouse SM22α promoter,

2) a transgenic mouse comprising a transgene construct comprising a nucleic acid sequence encoding mouse calreticulin (CRT) operably linked to a mouse SM22α promoter,

3) a method of making a transgenic mouse comprising a transgene construct comprising a nucleic acid sequence encoding mouse calreticulin (CRT) operably linked to a mouse SM22α promoter,

does not reasonably provide enablement for:

1) a transgene comprising a nucleic acid sequence encoding any species of calretuculin operably linked to any SM22a promoter from any species of animal,

2) a transgenic mouse comprising a transgene construct comprising a nucleic acid sequence encoding any species of calretuculin operably linked to any SM22a promoter from any species of animal,

3) a method of making a transgenic mouse comprising a transgene comprising a nucleic acid sequence encoding any species of calretuculin operably linked to any SM22a promoter from any species of animal.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record, May 6, 2005.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

With regards to the applicant pointing out that the art teaches that the SM22α promoter is well known in the art, that the art teaches the use of different SM22α promoter fragments, and that it would not be undue experimentation for an artisan to obtain promoter fragments known to have similar activity to the promoter element used in the instant application without experimentation, the Examiner finds the argument partly persuasive. While the argument is persuasive for obtaining any mouse SM22α promoter, the argument is not completely persuasive for a SM22α promoter from any animal. It is noted that the references provided by the Applicant (e.g. Hoggatt et al., Kim et al., and Ribault et al.) teach a mouse SM22α promoter and transgenic mice comprising a transgene construct comprising a mouse SM22α promoter, but do not teach SM22α promoters from other species of animal. A search on the NCBI website indicates that Soloway et al., 1995, JBC, 270: 13460-13469, teach a mouse SM22α promoter, wherein mouse SM22α promoter corresponds to NCBI accession number L41161 (see footnote on the bottom of page 13460 of Solway et al.) and the promoter is bases 1-1340 in the sequence provided by Soloway et al. (see NCBI printout for L41161, under "FEATURES" and "promoter"). A BLAST of the sequence provided by Soloway et al. does not provide other SM22α promoters from other species of animals. Further, given that the NCBI database also comprises genomic libraries and that no

genomic clones have been identified by the BLAST search, suggests that the sequence of the SM22α promoter from other species of animals are not highly conserved. In addition to this issue, in light of Cowan et al. teaching that promoters do not function predictably in other species of transgenic animals (see Office Action, May 6, 2005, pages 7-8), an artisan could not obtain any SM22a promoter based on the teachings of one example of a mouse SM22α promoter in a transgenic mouse without undue experimentation. Thus, the invention is limited to a mouse SM22α promoter.

In the case of the claims broadly encompassing the use of a nucleic acid sequence that encodes CRT, while the Applicant indicates that there is a high degree of identity amongst CRT sequences and asserts that related peptides would have similar function, the Examiner does not find the argument persuasive because the art (e.g. Hammer et al., page 9 of Office Action, May 6, 2005) teaches that heterologously expressed transgenes do not function predictably in other species of animals. The Applicant does not provide any guidance that CRT function is conserved in other heterologous species of animals such that an artisan would be enabled for the claim's broadest scope.

Claims 1, 3, 4, 12-17 remain rejected in part under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention for reasons of record, May 6, 2005.

Applicant's arguments filed August 29, 2005 have been fully considered but they are not fully persuasive.

For reasons similar to that described above in the enablement section above, while the Applicant provides a persuasive argument that an artisan could readily obtain a mouse SM22α promoter, the Applicant does not provide a persuasive argument that an artisan could readily obtain a SM22α promoter from any species of animal. While the art teaches a mouse SM22α promoter, the art does not teach what structure(s) or characteristics a SM22α promoter from any species of animal should have such that an artisan could obtain one.

With regards to the Applicant's argument concerning the scope of any calreticulin peptide, wherein the peptide has 60% homology to SEQ ID NO. 23, a BLAST search to mouse calreticulin teaches that at the time of filing, that calreticulin mRNA sequence for other species of mammals was well known at the time of filing. The art teaches that sequences such as that from dog and monkey are 87% similar to that of mouse calreticulin; however, the art does not teach sequences that have 60% identity and encode calreticulin. While the specification contemplates variants may be from a different species of animal which has 60% homology (specification, page 10, 2nd parag.) or that an artisan may envision that truncated proteins could be encompassed in the scope of the claims, the specification does not teach the characteristics (e.g. domains) of calreticulin, wherein 60% of the mouse calreticulin sequence would need to be

maintained such that the protein, when expressed in vascular smooth muscle, results in hemangioma formation. Thus, the claim is limited to only SEQ ID NO. 23.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15, 17-19 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15, as written, is drawn to a transgenic mouse and is dependent on claim 4. However, claim 4 is a method claim.

Claims 17-19 are unclear because the claims use the term, "corresponding to." "Corresponding to" is vague because there are no parameters associated with which nucleic acids and how many nucleic acids of the sequence need to correspond to SEQ ID NO. 1 and 12.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

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